



(72) KRAFT, Philip, CH
(71) GIVAUDAN-ROURE (INTERNATIONAL) SA, CH
(51) Int.Cl.⁶ C07D 321/00, A61K 7/46
(30) 1997/06/09 (97109303.4) EP
(54) **DIOXACYCLOALCAN-8-ONE**
(54) **DIOXACYCLOALKAN-8-ONE**

(57) Cette invention concerne des 1,7-dioxacycloalkan-8-ones comportant de 14 à 17 atomes dans le cycle et substituées en position 4 par un méthyle, et des 1,7-dioxacycloalkan-8-ones comportant de 14 à 16 atomes dans le cycle et disubstituées en position 4 par des méthyles, l'utilisation de ces composés comme agent odorant, ainsi qu'un procédé économique pour les produire.

(57) The invention is concerned with 14- to 17-membered 4-methyl substituted 1,7-dioxacycloalkan-8-ones and 14- to 16-membered 1,7-dioxacycloalkan-8-ones with 4,4-dimethyl substitution, the use of these compounds as odorants as well as an economical process for their manufacture.

0

Abstract

5

The invention is concerned with 14- to 17-membered 4-methyl substituted 1,7-dioxacycloalkan-8-ones and 14- to 16-membered 1,7-dioxacycloalkan-8-ones with 4,4-dimethyl substitution, the use of these compounds as odorants as well as an economical process for their manufacture.

10

The invention is concerned with 14- to 17-membered 4-methyl substituted 1,7-dioxacycloalkan-8-ones and 14- to 16-membered 4,4-dimethyl substituted 1,7-dioxacycloalkan-8-ones, the use of these compounds as odorants and a cost-effective process for their manufacture.

Warm, sweet-powdery bottom notes with musk-like olfactory properties, which can extend from *flowery-sweet* (musk ambrette) via *powdery-animalic* (musk ketone) to even *herby-woody* tonalites (musk xylene) are almost indispensable in the composition of a perfume as well in the perfuming e.g. of cosmetics, washing and cleaning agents, conditioners or air fresheners. Having regard to such olfactory characteristics and not least also because of their industrially simple and economical synthesis, aromatic musk substances have earned particular significance in perfumery and have been used universally and in high dosages. These compounds, especially musk xylene and musk ambrette, have, however, a certain toxicity, especially phototoxicity, and poor biological degradability. Depending on territorial regulations they should or must no longer be used in new creations and should or must also be replaced by other compounds in old creations.

Other compounds with musk-like olfactory properties, especially toxicologically harmless macrocycles, are, however, significantly more expensive and have, inter alia, other side notes. Accordingly, when a nitromusk is replaced by a macrocycle the overall olfactory impression of a composition usually changes substantially. Moreover, the macrocycles which are commercially available today are by far not as facet-rich as the series of aforementioned highly substituted aromatics.

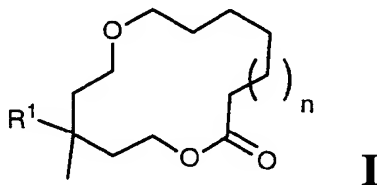
From the foregoing it will be evident that there exists a great need for novel toxicologically harmless macrocyclic compounds with novel olfactory notes, especially such which are reminiscent of aromatic musk substances or with which similar facet-rich perfumistic effects can be produced. Moreover, such macrocyclic compounds should be simple and economical to manufacture in order that they can be used not only in luxury perfumes, but also in products which are needed every day in the home, e.g. in cosmetics, washing and cleaning agents, conditioners or air fresheners.

- 2 -

0

The object of the present is to satisfy this need and to provide such compounds. Moreover, these compounds should be cost-effective to manufacture.

The object is achieved by the 4-methyl substituted 1,7-dioxacycloalkan-8-one class of compound, which satisfies the requisite demands in an ideal manner. They are represented by general formula I

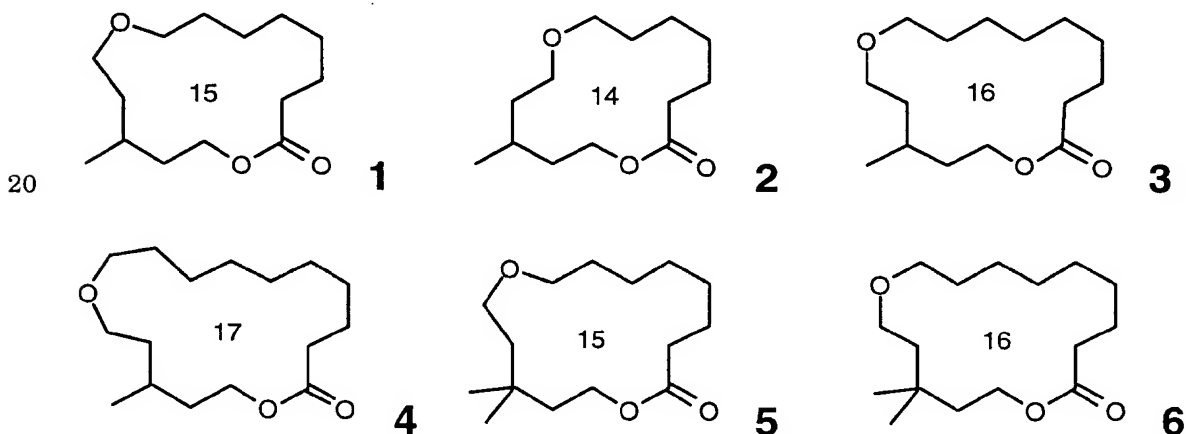


10

wherein
or

$R^1 = H$ and $n = 1-4$
 $R^1 = CH_3$ and $n = 1-3$.

The class of compound in accordance with the invention accordingly embraces the 14- to 17-membered 1,7-dioxacycloalkan-8-ones with methyl substitution in the 4-position and the 14- to 16-membered 1,7-dioxacycloalkan-8-ones with dimethyl substitution in the 4-position. The compounds with the following formulae 1-6 are examples of the novel class of compound, with the compounds having formulae 1, 3 and 4 being especially prominent organoleptically.



The compounds of general formula I have perfumistically interesting, *powdery-warm, for the most part musk-like olfactory notes with fresh-floral to herb-like accents* as well as a good adhesion and are biologically decomposable. They are capable, alone or in combination with other macrocyclic odorants, of replacing toxicologically questionable compounds with the same or similar

25

0 olfactory notes such as, for example, musk ambrette in the fields of use
 mentioned earlier. Further, having regard to their facet-rich olfactory
 properties, they give, not only individually but also in combination, interesting
 new effects in new compositions. The olfactory notes thereby extend from the
 14- to the 17-membered compounds from *weakly musk-like, anise-like, herby,*
 5 *saffron, myrrh to strongly musk-like animalic.* In particular, compounds 1, 3
 and 4 are especially striking in this respect.

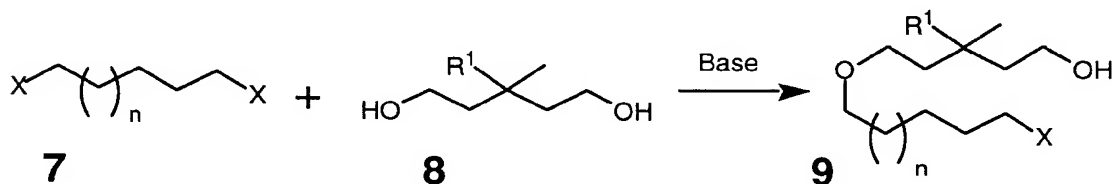
The compounds of general formula I harmonize with a large number of natural
 and synthetic products which are frequently used in odorant compositions.
 10 Especially in the chypre olfactory direction, for example in combination with a
 leathery accord, or in floral salicylate perfumes the compounds of general
 formula I give very interesting perfumistic effects. In particular, the
 compound 1 is ideally also suited for the composition of sweet fougère notes of
 the "Brut" (Fabergè, 1964) type and its more complex modern successors. The
 15 use is, however, limited neither to this type of perfume nor to special olfactory
 directions, odorants or classes of substance. Examples of classes of substance
 which harmonize especially well are:

- | | | |
|----|-------------------------------|---|
| 20 | - ethereal oils and extracts: | e.g. castoreum, costusroot oil, oak moss
absolute, geranium oil, jasmin absolute,
patouli oil, rose oil, sandalwood oil or ylang-
ylang oil; |
| 25 | - alcohols: | e.g. citronellol, Ebanol®, eugenol, geraniol,
Javanol®, linalool, phenylethyl alcohol,
Sandalore®, terpineol or Timberol®; |
| 30 | -aldehydes and ketones | e.g. <i>alpha</i> -amylcinnamaldehyde,
Georgywood®, hydroxycitronellal, Iso-E-
Super®, Isoraldein®, Hedion®, maltol,
methylcedryl ketone, methylionone or
vanillin; |
| 35 | - ethers and acetals: | e. g. Ambrox®, geranyl methyl ether, rose
oxide or Spirambrene®; |

- 0 – esters and lactones: e.g. benzyl acetate, cedryl acetate, γ -
decalactone, γ -undecalactone or vetiveryl
acetate;
- macrocycles: e.g. ambrettolide, Musk TM II® or
5 Exaltolid®;
- heterocycles: e.g. isobutylquinoline.

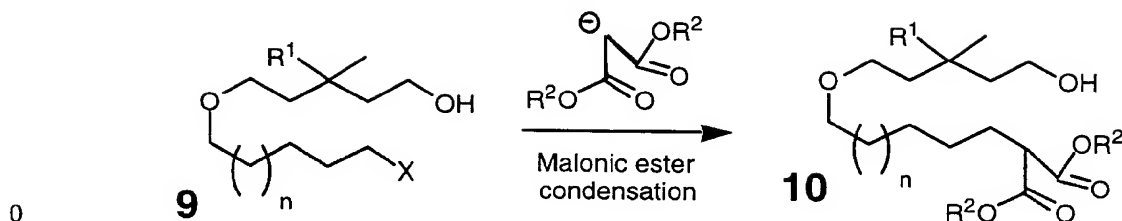
The object of the cost-effective synthesis of the compounds of general formula I is achieved in accordance with the invention by a new access which starts from aliphatic dihalides and diols, which are readily accessible and economical starting materials. The synthesis sequence is based on a novel one-pot reaction comprising decarboxylation and cyclization which enables aliphatic hydroxymalonic esters to be cyclized directly to 14- to 17-membered macrolides.

The novel synthesis sequence to 14- to 17-membered oxamacrolides, via which especially the compounds of general formula **I** are accessible economically, begins, as presented schematically hereinafter, with the Williamson reaction of an aliphatic dihalide **7** with $n = 1-4$ and $X = \text{Br}$ or Cl and a diol **8**, whereby $\text{R}^1 = \text{H}$ or Me for the synthesis of the compounds of general formula **I**, in the presence of a strong base, e.g. of sodium hydride. In addition to the dimeric condensation product **9** there are also obtained higher oligomers, which, however, do not interfere with the further reaction, and accordingly the intermediate **9** need not be purified. Preferably, unused starting materials **7** and **8** are, after the reaction, separated by distillation for re-use.

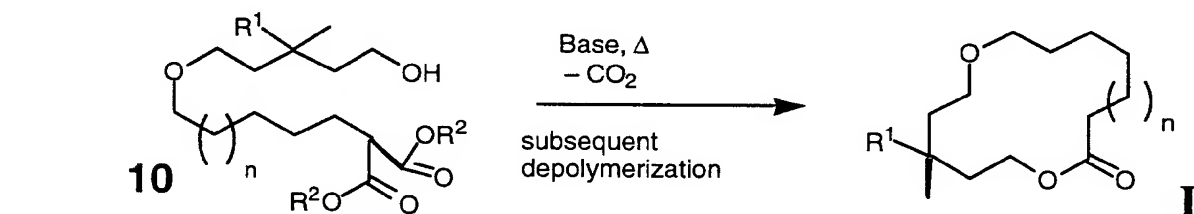


30 The next step of the sequence is a malonic ester condensation which is carried out in a manner known per se and which from the haloalcohol **9** yields the hydroxymalonic ester **10** in which R² = alkyl, preferably Me or Et.

- 5 -



In accordance with the invention the hydroxymalonic ester **10** is now without intermediary purification saponified in the novel one-pot reaction and polymerized with decarboxylation. The depolymerization and cyclization to the target compound, especially to a compound of general formula I, is effected by a process known per se, e.g. according to the process described in U.S. Patent 2234551, which is presented schematically hereinafter.



By the one-pot decarboxylation-polymerization and by the described synthesis sequence the use of expensive long-chain aliphatic halocarboxylic acids, which represents the major cost factor in the conventional synthesis of 14- to 17-membered oxamacroliides, is circumvented.

Although the described synthesis sequence is preferably directed to the manufacture of compound of general formula I, it can also be used in accordance with the invention for the economical manufacture of already known 14- to 17-membered oxamacroliides.

The compounds in accordance with the invention, preferably the compounds **1** to **6**, especially the compounds **1**, **3** and **4**, particularly the compound **1**, can be used individually or in combination as odorants. Particularly interesting olfactory effects are produced in an odorant composition when the respective compound is replaced by a content of about 0.1 to about 25 wt.%, preferably from 10 to 15 wt.%.

Further advantages, characteristics and particulars for illustrating the invention appear from the following description of preferred working examples:

0

Example 1: Manufacture of 12-methyl-9-oxa-14-tetradecanolide (1)

118 g (1.0 mol) of 3-methyl-1,5-pentanediol and 317 g (1.3 mol) of 1,6-dibromohexane in 2.5 l of dioxan were treated at room temperature with 28 g
 5 (1.1 mol) of 95 percent sodium hydride and subsequently heated under reflux for 24 h. After cooling the reaction mixture was treated with 400 ml of water, neutralized with saturated ammonium chloride solution and subsequently extracted three times with 1 l of *tert*-butyl methyl ether each time. The combined organic extracts were washed with saturated ammonium chloride
 10 solution, dried over magnesium sulphate and concentrated on a rotary evaporator. Starting material and byproducts were removed by distillation in a vacuum at 150°C bath temperature and 0.09 mbar. As the distillation residue there were obtained 183 g of 66 percent 12-bromo-3-methyl-6-oxadodecan-1-ol (43%), which is sufficiently pure for the further reactions.

15

A sample, purified by bulb tube distillation at 200°C/0.03 mbar, shows the following spectroscopic data:

IR (film): $\nu = 1112 \text{ cm}^{-1}$ ($\nu_{\text{as}} \text{ C-O-C}$), 1060 cm^{-1} ($\nu_{\text{s}} \text{ C-O-C}$), 3389 cm^{-1} ($\nu \text{ O-H}$), 1459 cm^{-1} ($\delta \text{ C-H}$), 1377 cm^{-1} ($\delta \text{ CH}_3$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.93$ (d, $J = 6.8 \text{ Hz}$, 3H, 3-Me), 1.35–1.49 (m, 6H, 2-, 9-, 10- H_2), 1.55–1.65 (m, 4H, 4-, 8- H_2), 1.72 (oct, $J = 6.8 \text{ Hz}$, 1H, 3-H), 1.89 (quint, $J = 6.8 \text{ Hz}$, 2H, 11- H_2), 2.19 (br s, 1H, OH), 3.39–3.49 (m, 6H, 5-, 7-, 12- H_2), 3.65 (ddd, $J = 10.4, 4.0$ and 4.0 Hz , 1H, 1- H_b), 3.71 (ddd, $J = 10.4, 3.7$ and 3.7 , 1H, 1- H_a). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta =$
 20 19.86 (q, 3-Me), 25.30 (t, C-9), 26.76 (d, C-3), 27.89 (t, C-10), 29.42 (t, C-8), 32.63 (t, C-12), 33.84 (t, C-11), 36.43 (t, C-4), 39.69 (t, C-2), 60.73 (t, C-1), 68.96 (t, C-5), 70.72 (t, C-7). – MS (EI): m/z (%) = 83 (100) [$\text{C}_6\text{H}_{11}^+$, 99 (61) [$\text{C}_6\text{H}_{11}\text{O}^+$, 117 (7), [$\text{M}^+ - \text{C}_6\text{H}_{12}\text{Br}$], 163 / 165 (6) [$\text{M}^+ - \text{C}_6\text{H}_{13}\text{O}_2$], 263 / 265 (2) [$\text{M}^+ - \text{OH}$].

30

A solution of 30 g (520 mmol) of 95 percent sodium methylate in 220 ml of dry methanol was heated to reflux. Thereupon, 60 ml (520 mmol) of dimethyl malonate were allowed to drop in, the reaction mixture was heated under reflux for a further 15 min. and then 182 g of 66 percent 12-bromo-3-methyl-6-oxadodecan-1-ol from the preceding batch were added thereto. After heating
 35 under reflux for 14 hours the reaction mixture was added to 1.6 l of water/*tert*-butyl methyl ether (1:1) and made acid with concentrated phosphoric acid. The organic phase was separated and the aqueous phase was extracted twice

0 with 500 ml of *tert*-butyl methyl ether each time. The combined organic phases were dried over magnesium sulphate, concentrated to dryness on a rotary evaporator, taken up in 400 ml of methanol and treated with 99 g (1.5 mol) of 85 percent potassium hydroxide. Methanol and byproducts were distilled off at 180°C/20-23 mbar during 1 h. Thereupon, the reaction mixture was treated
 5 with 200 ml (2.4 mol) of 3-chloro-1,2-propanediol and heated to 140°C for 1 h. After distilling off the excess 3-chloro-1,2-propanediol the reaction vessel was fitted with a condenser and separator and treated with 6.0 g (86 mmol) of potassium methylate in 450 ml of anhydrous glycerol. After stirring at 140°C/20-30 mbar for 15 minutes the mixture was heated to reflux at 155°C/4-
 10 6 mbar for 3 days under the separator, with 6.0 g (86 mmol) of potassium methylate being added every 24 hours. The separated glycerol was poured into 800 ml of water and extracted three times with 500 ml of *tert*-butyl methyl ether each time. After drying the combined organic extracts over magnesium sulphate, concentration on a rotary evaporator and distillation at 95-
 15 97°C/0.04 mbar there were obtained 59 g (52%) of 12-methyl-9-oxa-14-tetradecanolide (1) as a colourless liquid with the following characteristics.

Odour: *Musk, flowery-woody, sweet-powdery, slightly anise-like, fresh, reminiscent of myrrh to musk ambrette, musk seed oil and tonkin musk.* – IR (film): $\nu = 1735\text{ cm}^{-1}$ ($\nu\text{ C=O}$), $1116 / 1153\text{ cm}^{-1}$ ($\nu_{\text{as}}\text{ O-C-C}$), 1247 cm^{-1} ($\nu_{\text{as}}\text{ C-C(=O)-O}$), 1209 cm^{-1} ($\nu_{\text{as}}\text{ C-O-C}$), 1352 cm^{-1} ($\delta\text{ CH}_3$), 1054 cm^{-1} ($\nu_{\text{as}}\text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.94$ (d, $J = 6.4\text{ Hz}$, 3H, 12-Me), 1.27–1.76 (m, 14H, 3-H₂–7-H₂ and 11-,13-H₂), 1.89 (oct, $J = 6.7\text{ Hz}$, 1H, 12-H), 2.34 (t, $J = 6.4\text{ Hz}$, 2H, 2-H₂), 3.37–3.52 (m, 4H, 8-,10-H₂), 4.16 (ddd, $J = 11.2, 9.9$ and 3.3
 25 Hz, 1H, 14-H_b), 4.19 (ddd, $J = 11.2, 5.4$ and 5.2 Hz , 1H, 14-H_a). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta = 19.22$ (q, 12-Me), 24.46 (t, C-3), 24.95 (d, C-12), 25.92 (t, C-6), 27.02 / 28.12 / 28.44 (t, C-4,-5,-7), 33.89 (t, C-2), 35.45 / 36.62 (t, C-11,-13), 61.51 (t, C-14), 67.60 / 69.61 (t, C-8,-10), 173.91 (s, C-1). – MS (EI): m/z (%) = 55 (100) [C_4H_7^+], 83 (59) [$\text{C}_6\text{H}_{11}^+$], 99 (24) [$\text{C}_6\text{H}_{11}\text{O}^+$], 124 (31) [$\text{M}^+ - \text{H}_2\text{O} -$
 30 $\text{C}_6\text{H}_{12}\text{O}$], 141 (19) [$\text{M}^+ - \text{H}_2\text{O} - \text{C}_6\text{H}_{11}$], 213 (1) [$\text{M}^+ - \text{CHO}$], 242 (1) [M^+]. – $\text{C}_{14}\text{H}_{26}\text{O}_3$ (242.36): calculated C 69.38, H 10.81; found C 69.24, H 10.68.

The following compounds have been manufactured in an analogous manner using dihalides 6 of different length. For them there are therefore set forth
 35 only the spectroscopic data, the olfactory characteristics and the elementary analyses:

0 **Example 2: 11-Methyl-8-oxa-13-tridecanolide (2)**

Odour: *Saffron, anise-like, woody-flowery, piny-terpene like, fresh, slightly musk-like.* – IR (film): $\nu = 1734\text{ cm}^{-1}$ ($\nu\text{ C=O}$), $1123 / 1155\text{ cm}^{-1}$ ($\nu_{\text{as}}\text{ O-C-C}$), 1254 cm^{-1} ($\nu_{\text{as}}\text{ C-C(=O)-O}$), 1203 cm^{-1} ($\nu_{\text{as}}\text{ C-O-C}$), 1357 cm^{-1} ($\delta\text{ CH}_3$), 1056 cm^{-1} ($\nu_{\text{as}}\text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.96$ (d, $J = 6.8\text{ Hz}$, 3H, 11-Me), 1.15 (dddd, $J = 14.5, 10.0, 4.8$ and 2.4 Hz , 1H, 12- H_b), $1.25\text{--}1.79$ (m, 10H, 3- $\text{H}_2\text{--}6\text{--H}_2, 10\text{--H}_2$), 1.85 (dddd, $J = 14.5, 7.6, 7.3$ and 3.9 Hz , 1H, 12- H_a), 1.99 (m, 1H, 11-H), 2.31 (ddd, $J = 14.8, 8.3$ and 3.7 Hz , 1H, 2- H_b), 2.41 (ddd, $J = 14.8, 9.3$ and 3.7 Hz , 1H, 2- H_a), $3.33\text{--}3.50$ (m, 4H, 7-,9- H_2), 3.98 (ddd, $J = 11.2, 11.0$ and 2.4 Hz , 1H, 13- H_b), 4.53 (ddd, $J = 11.2, 4.6$ and 3.6 Hz , 1H, 13- H_a). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta = 19.47$ (q, 11-Me), 23.72 (d, C-11), $25.32 / 25.51 / 26.81$ (t, C-3–C-5), 28.62 (t, C-6), 33.79 (t, C-2), 34.53 (t, C-12), 36.51 (t, C-10), 60.96 (t, C-13), $66.91 / 68.85$ (t, C-7,-9), 173.78 (s, C-1). – MS (EI): m/z (%) = 55 (100) [C_4H_7^+], 83 (79) [$\text{C}_6\text{H}_{11}^+$], 101 (48) [$\text{C}_6\text{H}_{13}\text{O}^+$], 111 (24) [$\text{C}_6\text{H}_{13}\text{O}^+$], 127 (30) [$\text{M}^+-\text{C}_6\text{H}_{13}\text{O}$], 145 (4) [$\text{M}^+-\text{C}_6\text{H}_{11}$], 169 (2) [$\text{M}^+-\text{C}_2\text{H}_3\text{O}_2$], 199 (1) [M^+-CHO], 228 (1) [M^+]. – $\text{C}_{13}\text{H}_{24}\text{O}_3$ (228.33): calculated C 68.38, H 10.60; found C 68.55, H 10.57.

20 **Example 3: 13-Methyl-10-oxa-15-pentadecanolide (3)**

Odour: *Musk, animalic, warm-powdery, flowery, slightly after saffron.* – IR (film): $\nu = 1734\text{ cm}^{-1}$ ($\nu\text{ C=O}$), $1118 / 1151\text{ cm}^{-1}$ ($\nu_{\text{as}}\text{ O-C-C}$), 1250 cm^{-1} ($\nu_{\text{as}}\text{ C-C(=O)-O}$), 1357 cm^{-1} ($\delta\text{ CH}_3$), 1061 cm^{-1} ($\nu_{\text{as}}\text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.91$ (d, $J = 6.4\text{ Hz}$, 3H, 13-Me), $1.31\text{--}1.66$ (m, 15H, 3- $\text{H}_2\text{--}8\text{--H}_2, 12\text{--H}_2, 14\text{--H}_b$), 1.83 (ddt, $J = 19.1, 9.6$ and 5.0 Hz , 1H, 14- H_a), 1.93 (m, 1H, 13-H), 2.33 (dd, $J = 6.9$ and 6.2 Hz , 2H, 2- H_2), $3.34\text{--}3.52$ (m, 4H, 9-,11- H_2), 4.14 (ddd, $J = 11.0, 5.5$ and 5.0 Hz , 1H, 15- H_b), 4.21 (ddd, $J = 11.0, 10.0$ and 4.0 Hz , 1H, 15- H_a). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta = 18.22$ (q, 13-Me), $24.67 / 25.26$ (t, C-3,-7), 25.53 (d, C-13), $27.21 / 27.40 / 27.52$ (t, C-4,-5,-6), 28.68 (t, C-8), 34.67 (t, C-2), 35.49 (t, C-14), 37.01 (t, C-12), 61.74 (t, C-15), $67.67 / 70.16$ (t, C-9,-11), 173.93 (s, C-1). – MS (EI): m/z (%) = 55 (100) [C_4H_7^+], 83 (64) [$\text{C}_6\text{H}_{11}^+$], 99 (30) [$\text{C}_6\text{H}_{11}\text{O}^+$], 138 (25) [$\text{M}^+-\text{C}_6\text{H}_{14}\text{O}_2$], 155 (23) [$\text{M}^+-\text{C}_6\text{H}_{13}\text{O}$], 213 (2) [$\text{M}^+-\text{C}_2\text{H}_3\text{O}$], 227 (2) [M^+-CHO], 256 (1) [M^+]. – $\text{C}_{15}\text{H}_{28}\text{O}_3$ (256.39): calculated C 70.27, H 11.01; found C 70.26, H 11.09.

0 **Example 4: 14-Methyl-11-oxa-16-hexadecanolide (4)**

Odour: *Animalic, musk, sweet, erogenous, warm-powdery*. – IR (film): $\nu = 1735 \text{ cm}^{-1}$ ($\nu \text{ C=O}$), $1117 / 1151 \text{ cm}^{-1}$ ($\nu_{\text{as}} \text{ O-C-C}$), 1254 cm^{-1} ($\nu_{\text{as}} \text{ C-C(=O)-O}$), 1361 cm^{-1} ($\delta \text{ CH}_3$), 1060 cm^{-1} ($\nu_{\text{as}} \text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.92$ (d, $J = 6.8 \text{ Hz}$, 3H, 14-Me), 1.29–1.56 (m, 14H, 4-H₂–9-H₂, 13-H₂), 1.61–1.67 (m, 3H, 3-H₂, 15-H_b), 1.79 (ddt, 14.0, 8.4 and 5.2 Hz, 1H, 15-H_a), 1.87 (m_c, 1H, 14-H), 2.33 (dd, $J = 6.8$ and 6.0 Hz , 2H, 2-H), 3.34–3.50 (m, 4H, 10-,12-H₂), 4.15 (ddd, $J = 11.2$, 6.0 and 5.2 Hz , 1H, 16-H_b), 4.18 (ddd, $J = 11.2$, 8.4 and 4.4 Hz , 1H, 16H_a). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta = 18.54$ (q, 14-Me), 24.80 / 26.15 (t, C-3,-8), 26.17 (d, C-14), 27.31 / 27.66 / 27.79 / 28.22 (t, C-4–C-7), 29.15 (t, C-9), 34.02 (t, C-2), 35.57 (t, C-15), 37.00 (t, C-13), 62.14 (t, C-16), 68.05 / 70.77 (t, C-10,-12), 174.14 (s, C-1). – MS (EI): m/z (%) = 55 (100) [C_4H_7^+], 83 (71) [$\text{C}_6\text{H}_{11}^+$], 99 (33) [$\text{C}_6\text{H}_{11}\text{O}^+$], 113 (13) [$\text{M}^+ - \text{C}_{10}\text{H}_{21}\text{O}$], 153 (15) [$\text{M}^+ - \text{C}_6\text{H}_{13}\text{O}_2$], 169 (16) [$\text{M}^+ - \text{C}_6\text{H}_{13}\text{O}$], 171 (9) [$\text{C}_{10}\text{H}_{19}\text{O}_2^+$], 227 (1) [$\text{M}^+ - \text{C}_2\text{H}_3\text{O}$], 241 (2) [$\text{M}^+ - \text{CHO}$], 270 (1) [M^+]. – $\text{C}_{16}\text{H}_{30}\text{O}_3$ (270.41): calculated C 71.07, H 11.18; found C 71.37, H 11.13.

Example 5: 12,12-Dimethyl-9-oxa-14-tetradecanolide (5)

20 Odour: *Relatively weak, powdery musk-like, woody-herby*. – IR (film): $\nu = 1734 \text{ cm}^{-1}$ ($\nu \text{ C=O}$), $1117 / 1154 \text{ cm}^{-1}$ ($\nu_{\text{as}} \text{ O-C-C}$), 1252 cm^{-1} ($\nu_{\text{as}} \text{ C-C(=O)-O}$), 1366 cm^{-1} ($\delta \text{ CH}_3$), 1046 cm^{-1} ($\nu_{\text{as}} \text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta = 0.94$ (s, 6H, 12-Me₂), 1.31–1.42 (m, 6H, 4-H₂–6-H₂), 1.50–1.57 (m, 4H, 3-,7-H₂), 1.69 (t, $J = 7.2 \text{ Hz}$, 2H, 11-H₂), 1.71 (dd, $J = 10.0$ and 6.8 Hz , 2H, 13-H₂), 2.30 (t, $J = 6.6 \text{ Hz}$, 2-H₂), 3.39 (t, $J = 5.2 \text{ Hz}$, 8-H₂), 3.46 (t, $J = 6.2 \text{ Hz}$, 10-H₂), 4.16 (t, $J = 7.0 \text{ Hz}$, 2H, 14-H₂). – $^{13}\text{C-NMR}$ (CDCl_3): $\delta = 23.72$, 24.91 (t, C-3,-6), 26.41 / 27.89 (t, C-4,-5), 28.59 (2q, 12-Me₂), 29.05 (t, C-7), 31.77 (s, C-12), 34.59 (t, C-2), 38.86 / 40.57 (t, C-11,-13), 61.93 (t, C-14), 67.66 / 69.88 (t, C-8,-10), 174.15 (s, C-1). – MS (EI): m/z (%) = 55 (100) [C_4H_7^+], 69 (72) [C_5H_9^+], 81 (40) [C_6H_9^+], 97 (59) [$\text{C}_6\text{H}_9\text{O}^+$], 113 (27) [$\text{C}_7\text{H}_{13}\text{O}^+$], 125 (27) [$\text{C}_8\text{H}_{13}\text{O}^+$], 141 (15) [$\text{M}^+ - \text{C}_6\text{H}_9\text{O} - \text{H}_2\text{O}$], 183 (2) [$\text{M}^+ - \text{C}_4\text{H}_7 - \text{H}_2\text{O}$], 227 (1) [$\text{M}^+ - \text{CHO}$], 256 (1) [M^+]. – $\text{C}_{15}\text{H}_{28}\text{O}_3$ (256.39): calculated C 70.27, H 11.01; found C 70.15, H 10.87.

Example 6: 13,13-Dimethyl-10-oxa-15-pentadecanolide (6)

35

Odour: *relatively weak, fruity-musk like, reminiscent of ambrettone*. – IR (film): $\nu = 1734 \text{ cm}^{-1}$ ($\nu \text{ C=O}$), $1118 / 1150 \text{ cm}^{-1}$ ($\nu_{\text{as}} \text{ O-C-C}$), 1242 cm^{-1} ($\nu_{\text{as}} \text{ C-C(=O)-O}$), 1365 cm^{-1} (d CH_3), 1055 cm^{-1} ($\nu_{\text{as}} \text{ C-O-C}$). – $^1\text{H-NMR}$ (CDCl_3): $\delta =$

- 10 -

0 0.95 (s, 6H, 13-Me₂), 1.33–1.40 (m, 8H, 4-H₂–7-H₂), 1.49–1.55 (m, 4H, 8-,12-H₂), 1.62 (m_c, 2H, 3-H₂), 1.76 (t, *J* = 8.0 Hz, 2H, 14-H₂), 2.32 (t, *J* = 6.4 Hz, 2H, 2-H₂), 3.38 (t, *J* = 5.2 Hz, 2H, 11-H₂), 3.47 (t, *J* = 5.8 Hz, 2H, 9-H₂), 4.16 (t, *J* = 8.0 Hz, 2H, 15-H₂). – ¹³C-NMR (CDCl₃): δ = 23.94 / 24.56 (t, C-3,-7), 25.84 / 26.36 / 26.52 (t, C-4,-5,-6), 28.04 (2q, 13-Me₂), 29.23 (t, C-8), 31.79 (s, C-13),
 5 34.53 (t, C-2), 39.02 (t, C-14), 41.28 (t, C-12), 61.98 (t, C-15), 67.82 / 70.49 (t, C-9,-11), 173.83 (s, C-1). – MS (EI): *m/z* (%) = 55 (100) [C₄H₇⁺], 69 (92) [C₅H₉⁺], 113 (39) [C₈H₁₇⁺], 139 (29) [M⁺–C₇H₁₅O₂], 155 (18) [M⁺–C₇H₁₅O], 197 (3) [M⁺–CO–C₂H₄O], 241 (2) [M⁺–CO], 270 (1) [M⁺]. – C₁₆H₃₀O₃ (270.41): calculated C 71.07, H 11.18; found C 70.89, H 11.11.

10

Example 7:

A masculine perfume composition "Oriental Fougere" was produced. The components are listed below. For this, 15 wt.% of compound 1 were used in
 15 place of the musk ambrette which is usual for this type of perfume composition. The composition contains no polycyclic musk odorants.

Compound 1 confers to the perfume a musk note, introduces sweetish-powdery effects reminiscent of nitromusk and therefore becomes more than a substitute
 20 for nitromusk. Its powderiness together with the tonkin musk aspect underlines the warm-powdery olfactory impression and contributes to the rounding-off of the top note and of the total composition.

Composition:		
25	Ingredients	Weight ‰
	1. Aldehyde C11 (10-undecen-1-al)	0.05
	2. Aldehyde C12 (lauric)	0.05
	3. α-Amyl cinnamic aldehyde	1.0
	4. Isoamyl salicylate	60.0
30	5. Anisic aldehyde	30.0
	6. Benzyl acetate extra	20.0
	7. Benzyl salicylate	80.0
	8. Bergamot oil Italian	100.0
	9. Citronellyl formate	5.0
35	10. Civet oil	1.0
	11. Coumarin pure crystalline	7.0
	12. Diethyl phthalate	1.8
	13. Dipropylene glycol	129.9

- 11 -

0	14. Geraniol extra	3.0
	15. Geranium oil African	70.0
	16. Heliotropin crystalline	30.0
	17. Hydroxycitronellal	90.0
	18. Lavender oil	50.0
5	19. Lemon oil Italian	50.0
	20. Lemongrass oil rectified	5.0
	21. Linalool synthetic	5.0
	22. Linalyl acetate synthetic	5.0
	23. Methyl anthranilate extra	3.0
10	24. Methyl β -naphthyl ketone	3.0
	25. γ -Undecalactone	0.1
	26. Petitgrain oil Paraguay pure	20.0
	27. Phenyl acetaldehyde 85%/PEA	0.1
	28. Phenyl ethyl alcohol white	15.0
15	29. Sandalwood oil East Indian	20.0
	30. Tarragon oil	25.0
	31. Terpineol pure	3.0
	32. Vanillin	7.0
	33. Vetiver oil (Bourbon)	10.0
20	34. Compound 1	<u>150.0</u>
		1000.0

Example 8:

25 A masculine perfume composition "Fresh Musk" was produced. 10 wt.% of compound 1 were used in analogy to Example 7. The components are listed below.

30 Compound 1 intensifies the musk character and adds a note reminiscent of nitromusk. The additional myrrh-jasmone aspect moderates the herb-spicy top note and thereby gives it completely new facets. Thus, compound 1 harmonizes very well and synergistically with other macrocyclic musk odorants, e.g. especially with cyclopentadecanolide, and can combine well with flowery notes such as e.g. jasmin.

35

- 12 -

0	Composition:	
	<u>Ingredients</u>	<u>Weight ‰</u>
	1. Agrudor BAV 645/3	15.0
	2. Ambretone (Musk TM II)	4.0
	3. Benzyl acetate extra	5.0
5	4. Benzyl salicylate	120.0
	5. Cepionate (Hedione)	5.0
	6. Dipropylene glycol	480.0
	7. Ethylene brassylate	200.0
	8. Hexyl cinnamic aldehyde	25.0
10	9. Lavandin oil (Grosso)	5.0
	10. Lemon oil Italian	5.0
	11. Linalyl acetate synthetic	25.0
	12. Cyclopentadecanolide	10.0
	13. Tonka bean resinoid N.1 30%/DPG	1.0
15	14. Compound 1	<u>100.0</u>
		1000.0

Example 9:

20 A perfume oil with a modern lavender note, rounded off by fine flowery musk-like woody tones, for use in soaps was produced; it contained 10 wt.% of compound 1 in place of nitromusk otherwise usually used for this olfactory type.

25 The components of the composition are listed hereinafter.

The composition confers to the soap a very warm-powdery, pleasant effect, which, when the soap is used, underlines the cleansing and caring character.

- 13 -

0	Composition:	
	<u>Ingredients</u>	<u>Weight %o</u>
	1. Acetaldehyde phenethylpropyl acetal	
	10% DPG	25.0
5	2. Allyl phenoxy acetate	5.0
	3. Aldehyde C10 (n-decanal)	6.0
	4. Aldehyde C11 (10-undecenal) 10% DPG	10.0
	5. Aldehyde C12 (lauric)	10.0
	6. Aldehyde C12 NMA 10 % DPG	32.0
10	7. Allyl amyl glycolate	8.0
	8. Allyl caproate	3.0
	9. Bergamyl acetate	25.0
	10. Cinnamic aldehyde	2.0
	11. Citronellal	5.0
15	12. Citronellol 750	30.0
	13. Coumarin pure crystalline	5.0
	14. Cyclamen aldehyde extra	5.0
	15. Dihydromyrcenol	110.0
	16. Ethyl vanillin 10% DPG	5.0
20	17. Eucalyptol	5.0
	18. Eugenol pure	5.0
	19. 3,6-Dimethyl- β -resocin acid methyl ester	2.0
	20. Florhydral	5.0
	21. Fructose	5.0
25	22. Galbanum oil 10% DPG	15.0
	23. Geranitril T	15.0
	24. Geranium oil African	15.0
	25. α -Hexyl cinnamic aldehyde	70.0
	26. 2,4,6-Trimethyl-3-cyclohexene-1-	
30	carboxaldehyde	9.0
	27. Lavender oil (Grosso)	15.0
	28. Lilial	120.0
	29. Lime oxide	10.0
	30. Linalool synthetic	20.0
35	31. Menthanyl acetate	25.0
	32. Menthyl acetate	15.0
	33. <i>para-tert</i> -Butylcyclohexyl acetate	60.0
	34. Patchouli oil	18.0

- 14 -

0	35. Phenyl ethyl acetate	10.0
	36. Phenyl ethyl alcohol white	30.0
	37. Rose oxide CO 10% DPG	5.0
	38. Rosemary oil	5.0
	39. Spearmint oil FCC NF extra	
5	KPF 10% DPG	10.0
	40. Terpineol pure	50.0
	41. Terpinyl acetate	15.0
	42. Tricyclal 10% DPG	10.0
	43. Tridecenonitrile 10% DPG	10.0
10	44. Verdol 10% DPG	15.0
	45. <i>ortho-tert</i> -Butylcyclohexyl acetate	10.0
	46. 1-Methyl-4-(4-methyl-3-pentenyl)-3-cyclohexene-1-carboxaldehyde	15.0
	47. Compound 1	<u>100.0</u>
15		1000.0

Analogous compositions to the compositions described in Examples 7 to 9 were also produced with compounds 3 and 4.

20

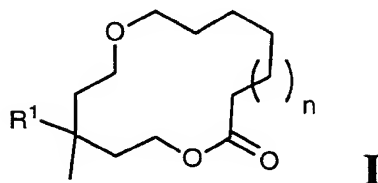
From all of these exemplified compositions it will be evident that the class of compound in accordance with the invention, especially at least of one of compounds 1, 3 and 4, preferably compound 1, is outstandingly suitable for use as odorants.

25

- 15 -

Claims

1. Compounds of general formula I



wherein $R^1 = H$ and $n = 1-4$
 or $R^1 = CH_3$ and $n = 1-3$

2. 12-Methyl-9-oxa-14-tetradecanolide (1).

3. 11-Methyl-8-oxa-13-tridecanolide (2).

4. 13-Methyl-10-oxa-15-pentadecanolide (3).

5. 14-Methyl-11-oxa-16-hexadecanolide (4).

6. 12,12-Dimethyl-9-oxa-14-tetradecanolide (5).

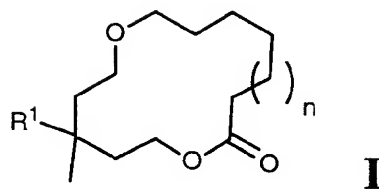
7. 13,13-Dimethyl-10-oxa-15-pentadecanolide (6).

8. The use of at least one of the compounds in accordance with claims 1 to 7 as an odorant, preferably at least one of the compounds in accordance with claims 2 to 7, especially at least of the compounds in accordance with claims 2, 4 and 5.

9. The use according to claim 8, wherein the compound is 12-methyl-9-oxa-14-tetradecanolide (1).

10. An odorant composition containing at least one of the compounds of formula I

- 16 -



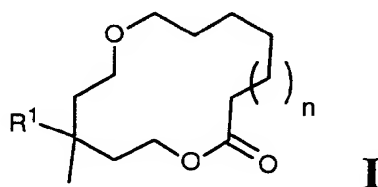
wherein $R^1 = H$ and $n = 1-4$
 or $R^1 = CH_3$ and $n = 1-3$,

preferably containing at least one of the compounds in accordance with claims 2 to 7, especially at least one of the compounds in accordance with claims 2, 4 and 5.

11. An odorant composition according to claim 10 containing the compound 12-methyl-9-oxa-14-tetradecanolide (1).

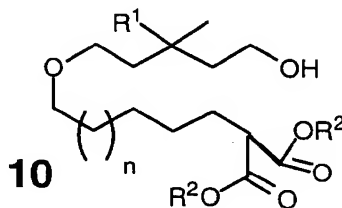
12. An odorant composition according to claim 10 or 11, wherein the compounds are present therein to about 0.1 to about 25%, preferably to 10 to 15%.

13. A process for the manufacture of a compound of general formula I



wherein $R^1 = H$ and $n = 1-4$
 or $R^1 = CH_3$ and $n = 1-3$,

which process comprises polymerizing the hydroxymalonic ester **10**



wherein $n = 1-4$ and $R^2 = \text{alkyl}$, preferably methyl or ethyl.

- 17 -

0

14. A process according to claim 13, wherein the polymerization is effected with decarboxylation.

Edmonton, Alberta, Canada,
Ottawa, Canada
Patent Agents